Amendments to the Claims

This listing of claims will replace all prior versions, and listings, of claims in the application.

Listing of Claims

1. (Currently amended) A pharmaceutical composition for the treatment of a disease involving active angiogenesis which comprises a tubulin binding agent together with an inhibitor of the formation of nitric oxide in a mammalian system and a pharmaceutically acceptable excipient.

2. (Currently amended) A pharmaceutical composition for the damage of the formation of new vasculature by angiogenesis comprising a combination of a tubulin binding agent [and], an inhibitor of nitric oxide synthase in an amount sufficient to augment the effect of the tubulin binding agent and a pharmaceutically acceptable excipient.

3. (cancelled)

4. (Previously submitted) A composition according to claim 2 wherein the inhibitor of nitric oxide synthase is selected from a derivative of arginine, ~~ortnithine~~ ornithine, lysine, citrulline, S-alkylthioureas and aminoguanidine.

5. (Original) A composition according to claim 4 wherein the nitric oxide synthase inhibitor is an N^G-substituted L-arginine selected from N^G-nitro-L-arginine and alkyl esters thereof, N^G-methyl-L-arginine and N^G-amino-L-arginine.

6. (Original) A composition according to claim 4 wherein the derivative of ornithine is L-N6-(1iminoethyl)-ornithine.

7. (Original) A composition according to claim 4 wherein the derivative of lysine is L-N6-(1-iminoethyl)-lysine.

8. (Previously submitted) A composition according to claim 4 wherein the derivative of citrulline is selected from L-thiocitrulline, L-homothiocitrulline or an S-alkylthiocitrulline.

9. (Cancelled).

10. (Currently amended) A composition according to claim 1 wherein the composition is in the form of a kit, one part of the kit containing the tubulin binding agent and the second part of the kit the inhibitor of the formation of nitric oxide ~~inhibitor~~.

11. (cancelled)

12. (cancelled)

13.(Previously submitted) A method of treatment for a mammal having a disease involving active angiogenesis said method comprising administration of a tubulin binding agent and an inhibitor of formation of nitric oxide in an amount sufficient to augment the effect of the tubulin binding agent.

14. (Currently amended) A method according to claim 13 wherein the tubulin binding agent and inhibitor of the formation of nitric oxide ~~inhibitor~~ are administered substantially simultaneously but separately to the mammal under treatment.

15. (cancelled)

16. (canceled)

17. (Cancelled)

18.(Canceled)

19. (Cancelled)

20. (Cancelled).

21. (Previously submitted) A composition according to claim 4 wherein the derivative of citrulline is S-methyl-L-thiocitrulline.

22.(Canceled)

23. (Canceled)

24. (Currently amended) A composition according to claim 1 or claim 2 wherein the tubulin binding agent is selected from N-acetylcolchinol and its prodrugs.

25. (Currently amended) A composition according to claim 1 or claim 2 wherein the tubulin binding agent is N-acetylcolchinol-O-phosphate.

26. (New) A composition according to claim 1 or claim 2 wherein the tubulin binding agent is selected from combretastatin A4 and its prodrugs.

27. (New) A composition according to claim 1 or claim 2 wherein the tubulin binding agent is selected from combretastatin A4 phosphate.

28. (New) A composition according to claim 1 or claim 2 wherein the tubulin binding agent is selected from (Z)-2 methoxy-5-[2-(3,4,5-trimethoxyphenyl)vinyl]phenylamine and its prodrugs.

29. (New) A composition according to claim 2 wherein the inhibitor of nitric oxide synthase is an aminopyridin .

30. (New) A composition according to claim 2 wherein the inhibitor of nitric oxide synthase

is 2-amino-4-methylpyridine.

31. (New) A composition according to claim 2 wherein the tubulin binding agent is selected from N-acetylcolchinol and its prodrugs, or combretastatin A4 and its prodrugs and wherein the inhibitor of nitric oxide synthase is selected from N^G-nitro -L-arginine or an alkyl ester thereof, N^G-methyl-L-arginine, N^G-amino-L-arginine, L-N6-(1-iminoethyl)ornithine, L-N6-(1-iminoethyl)-lysine, L-thiocitrulline, L-homothiocitrulline, S-akylthiocitrulline and 2-amino-4-methylpyridine.

32. (New) A composition according to claim 2 wherein the tubulin binding agent is selected from N-acetylcolchinol and its prodrugs, or combretastatin A4 and its prodrugs, and wherein the inhibitor of nitric oxide synthase is selected from N^G-nitro-L-arginine or an alkyl ester thereof and 2-amino-4-methylpyridine.

33. (New) A method of treatment for a mammal having a cancer involving a solid tumor said method comprising ad administration of a tubulin binding agent and an inhibitor of the formation of nitric oxide in an amount sufficient to augment the effect of the tubulin binding agent.

34. (New) A method according to claim 33 wherein the tubulin binding agent and the inhibitor of the formation of nitric oxide are administered substantially simultaneously but separately to the mammal under treatment.

35. (New) A method according to claim 13 or claim 33 wherein the inhibitor of the formation of nitric oxide is an inhibitor of nitric oxide synthase.

36. (New) A method according to claim 35 wherein the inhibitor of nitric oxide synthase is selected from a derivative of arginine, ornithine, lysine, citrulline, S-alkylthioureas and aminoguanidine.

37. (New) A method acc according to claim 35 wherein the inhibitor of nitric oxide synthase is an N^G-substituted L-arginine selected from N^G-nitro-L-arginine and alkyl esters thereof, N^G and N^G ino-L-arginine.

38. (New) A method according to claim 37 wherein the derivative of ornithine is L-N6-(1--iminoethyl)-ornithine.

39. (New) A method according to claim 37 wherein the derivative of lysine is L-N6-(1-iminoethyl)-lysine.

40. (New) A method according to claim 37 wherein the derivative of citrulline is selected from L-thiocitrulline, L-homothiocitrulline or an S-alkylthiocitrulline.

41. (New) A method according to claim 35 wherein the inhibitor of nitric oxide synthase is an aminopyridine.

42. (New) A method according to claim 35 wherein the inhibitor of nitric oxide synthase is 2-amino-4-methylpyridine.

43. (New) A method according to claim 13 or claim 33 wherein the tubulin binding agent is selected from N-acetylcolchinol and its prodrugs.

44. (New) A method according to claim 13 or claim 33 wherein the tubulin binding agent is N-acetylcolchinol-O-phosphate.

45. (New) A method according to claim 13 or claim 33 wherein the tubulin binding agent is selected from combretastin A4 and its prodrugs.

46. (New) A method according to claim 13 or claim 33 wherein the tubulin binding agent is selected from combretastain A4 phosphate.

47. (New) A method according to claim 13 or claim 33 wherein the tubulin binding agent is selected from (Z)-2-methoxy-5-[2-(3, 4, 5-trimethoxyphenyl)vinyl]phenylamine and its prodrugs.

48. (New) A method according to claim 35 wherein the tubulin binding agent is selected from N-acetylcolchinol and its prodrugs, or combretastatin A4 and its prodrugs and wherein the inhibitor of nitric oxide synthase is selected from N^G-nitro-L-arginine or an alkyl ester thereof, N^G-methyl-L-arginine, N^G-amino-L-arginine, L-N6-(1-iminoethyl)-ornithine, LN6-(1-iminoethyl)-lysine, L-ihiocitrulline, L-homothiocitrulline, S-alkylthiocitrulline and 2--amino-4-methylpyridine.

49. (New) A method according to claim 35 wherein the tubulin binding agent is selected from N-acetylcolchinol and is prodrugs, or combretastatin A4 and its prodrugs, and wherein the inhibitor of nitric oxide synthase is selected from N^G-nitro-L-arginine or an alkyl ester thereof and 2-amino-4-methylpyridine.